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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,054	CHILKOTI ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *15,20,22-27 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-19,21,28-46 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/10/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

In the original restriction requirement, applicant was required to make an election of species such that each of the following elements were particularly identified: article, surface portion, linking layer bonding type, linking layer architecture (Note: no election was made by applicant for this element), anchoring group, initiator, spacer, deposition technique for anchoring layer, protein-resistant head group, and core vinyl monomer. This requirement is hereby modified such that identification of a particular article, protein-resistant head group, and surface portion are sufficient for defining the species under examination. Based upon the election previously made by applicant, the article is an orthopedic implant, the protein-resistant head group is tri(sarcosine), and the surface portion comprises metal.

Claims 15, 20, 22-27, and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14, 16-19, 21, 28-46, and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 33 recite the limitation "...a plurality of branches formed from said hydrophilic head group projecting from said stem" in lines 9-10 and lines 10-11, respectively. There is insufficient antecedent basis for the limitation "said hydrophilic group" in the claims. The remaining claims recited in the statement of rejection are dependent from these claims and are similarly indefinite.

For the sake of application of prior art, this limitation is interpreted as "said protein-resistant head group"

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-9, 12-14, 18-19, 21, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. (US PGPub No. 2002/0102405).

Broadly, the invention of claims 1-4, 6-9, 12-14, 18, 21, and 32 is a device (article) with polymer brushes on its surface that are attached to the device surface via a linking layer. These polymer brush bristles have protein resistant groups (kosmotropes) that confer protein resistance to the surface of the device. Chapman et al. teach this concept (see figure 1 and paragraphs 114-117; instant claim 1). A self assembled monolayer of alkanethiol is formed on an article that is coated with gold (see paragraph 153 and 159; instant claims 2-4 and 6). The exposed end is converted into a reactive functional group (initiator terminated alkanethiol) such that a polymer can be grafted (see paragraph 153; instant claim 7). This polymer contains several head groups (branches) that resist the adsorption of proteins (see paragraph 153 and 162). Functional groups other than the acetoamido groups exemplified are taught to also

serve as head groups on the polymer (see paragraph 115 and 196). Chapman et al. teach such coatings for articles that are in-dwelling, such as artificial bone or joint replacements (orthopedic implant) (see paragraph 64; instant claim 21). Chapman et al. also teach self assembled monolayers that display different protein resistant head groups. In the set demonstrated to be particularly effective is tri(sarcosine) (see figures 4-5 and paragraph 144; instant claims 12-14). Chapman et al. go on to teach that in addition to protein resistance, their polymer layers can be further modified by covalently attaching ligands that bind specific biomolecules (receptor) (see paragraph 124; instant claim 18-19). Protein molecules are particularly envisioned (see paragraph 121; instant claim 18). Upon exposure to fluid with biomolecules, adsorption of general biomolecules (e.g. protein) is resisted such that only binding of those biomolecules for which the ligand is specific occurs (see paragraph 124; instant claim 32).

Claims 1 and 8-9 recite a product-by-process. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. In the instant case, these claims do not add any structural limitation to the invention. Thus in view of the teachings of Chapman et al., it would have been obvious to one of ordinary skill in the art at the time of the invention to select tri(sarcosine) as the protein resistant head group to include in the surface bound

polymer of their invention, where an orthopedic implant is the coated article and gold is in the metal layer linking the polymer to the article substrate. Further the use of their invention where a protein capable of binding a particular biomolecule is attached to the polymer to selectively capture this biomolecule from a biological fluid, while repelling the binding of other proteins, would also have been obvious based upon the teachings of Chapman et al. Therefore claims 1-4, 6-9, 12-14, 18-19, 21, and 32 are obvious over Chapman et al.

Claims 1 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. as applied to claims 1-4, 6-9, 12-14, 18-19, 21, and 32 above, and further in view of Healy (Current Opinion in Solid State and Materials Science (1999 4:381-387).

Chapman et al. make obvious an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles (see instant claims 1-4, 6-9, 12-14, 18, 21, and 32). This reference does not explicitly teach that the article is exposed to a particular biological fluid for a specified period of time.

Healy teaches that it was known at the time of the invention to covalently link RGD peptide sequences to the surface of protein resistant coatings to facilitate certain cell interactions (see page 383 column 2 paragraph 1). In particular these methods were envisioned for metal and polymer medical implants to facilitate wound healing (see page 348 column 1 paragraph 1). Wound healing would be an issue post-implantation where the implant contacts blood (e.g. orthopedic implant) and when it is present for a

prolonged period (e.g. greater than one day). Thus it would have been obvious for one of ordinary skill in the art at the time of the invention to implant (*in vivo* contacting) the orthopedic device made obvious by Chapman et al. for longer than one day wherein during this period it was in contact with biological fluid and resisted protein adsorption. Therefore claims 1 and 28-31 are obvious over Chapman et al. in view of Healy.

Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. as applied to claims 1-4, 6-9, 12-14, 18-19, 21, and 32 above, and further in view of Leckband et al. (Journal of Biomaterials Science Polymer Edition 1999 10:1125-1147).

Chapman et al. make obvious an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles (see instant claims 1-4, 6-9, 12-14, 18, 21, and 32). This reference does not explicitly teach the surface density of polymer. Leckband et al. teach polymer brushes on a substrate as a protein resistant surface (see abstract). In particular, Leckband et al. discuss that the graft density (polymer surface density) is a key parameter in controlling the degree of protein adsorption retardation (see page 1143 paragraph 4). Although Leckband et al. do not provide precise mass per area values for this parameter, they do teach that it is optimized based upon the target environment (e.g. size, geometry and concentration of proteins) (see page 1143 paragraph 4). Thus it would have been well within the purview of one of ordinary skill in the art to optimize such a parameter as a matter of routine

experimentation. Therefore claims 1 and 17 are obvious over Chapman et al. in view of Leckband et al.

Claims 1-14, 16, 18-19, 21, 33-39, 41-46, 48, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. as applied to claims 1-4, 6-9, 12-14, 18-19, 21, and 32 above, and further in view of Hawker et al. (US Patent No. 6,413,587 - see IDS), and Zhang et al. (Biomaterials 1998 19:691-700).

Chapman et al. make obvious an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles (see instant claims 1-4, 6-9, 12-14, 18, 21, and 32). This reference does not explicitly teach that the polymer is formed by the surface initiated polymerization of monomers with a core monomer group and a protein resistant head group coupled thereto, the polymerization of their taught polymer from the substrate surface, or that the linking layer is patterned on the substrate.

Zhang et al. teach a polymer brush utilized to resist protein adhesion on implant surfaces (see page 691 column 1 paragraph 10). Specifically these polymers are composed of monomers of methacryloyloxyethyl phosphorylcholine, an acrylate monomer with a coupled phosphorylcholine group, and butyl methacrylate (see page 691 column 2 paragraph 1 and page 700 column 1 paragraph 2; instant claims 10-11 and 42-43). Chapman et al. teach phosphorylcholine as an envisioned protein resistant head group whose performance in this capacity was not as good as tri(sarcosine) (see Chapman et al. figure 5).

Hawker et al. teach polymer brush patterns built from a self assembled monolayer on a substrate (see abstract; instant claims 38). In particular, a substrate surface that can be composed of a variety of envisioned materials (e.g. gold or tungsten) serves as the base for the polymer (see column 8 lines 9-18; instant claims 34-35). Subsequently a compound (linking layer) containing a group reactive with the substrate surface on one end and providing an initiator on the other end is applied to the surface (see column 8 lines 56-67 and column 9 lines 27-29). The material is then contacted with a polymerizable composition composed of monomers that sequentially form polymers at these initiation sites (see column 9 lines 60-64). One preferred technique utilizes an initiator that generates a free radical polymerization and vinyl monomers (see column 10 lines 10-17; instant claims 1, 9-10, 33, and 41-42). The resulting polymers are taught to be between 28 and 38 nm in length (see figure 3; instant claims 17 and 48). This technique is taught in particular in the production of patterned surfaces, where the initiator containing molecules are placed in particular locales on the substrate (see column 8 lines 53-64; instant claims 5 and 37). In one example, Hawker exemplifies the compound that makes up the linking layer as an initiator terminated alkanethiol that forms a patterned or continuous self assembled monolayer (column 13 lines 46-50 and 58-63; instant claims 4-7 and 36-39).

Based upon these teachings it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare an orthopedic implant with the polymer layer of Chapman et al. via the method of Hawker et al. using an acrylate monomer coupled with tri(sarcosine) instead of the phosphorylcholine as taught by Zhang et al.

(see instant claims 44-46). A free radical polymerization initiated from a self assembled monolayer of initiator-terminated alkanethiols on a gold surface would follow from this combination of references (see instant claim 48). Further modification of the resulting layer of polymer brush molecules by covalently attaching a protein (ligand), based upon the teachings of Chapman et al., would also have been obvious (see instant claims 18 and 50). Therefore claims 1-14, 16, 18-19, 21, 33-39, 41-46, 48, and 50 are obvious over Chapman et al. in view of Zhang et al. and Hawker et al.

Claims 33 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. in view of Zhang et al. and Hawker et al. as applied to claims 1-14, 16, 18-19, 21, 33-39, 41-46, 48, and 50 above, and further in view of Guan et al. (US Patent No. 6,071,980)

Chapman et al. in view of Zhang et al. and Hawker et al. make obvious a method of making an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles, wherein the polymer brush is formed via surface initiated polymerization of monomers with a core monomer group and a protein resistant head group coupled thereto (see instant 33). This modified reference does not explicitly teach that the polymerization is carried out via atom transfer radical polymerization.

Guan et al. teach that although it is know to polymerize vinyl monomers via free radical polymerization, atom transfer radical polymerization is also a via means of polymerizing these same monomers (see column1 lines 58-59 and column 2 lines 10-

19). Thus as a known option within their technical grasp, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ atom transfer radical polymerization as the polymerization method instead of free radical polymerization in the invention of Chapman et al. in view of Zhang et al. and Hawker et al., where vinyl monomers are used as the core group. Therefore claims 33 and 40 are obvious over Chapman et al. in view of Zhang et al., Hawker et al., and Guan et al.

Claims 33 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. in view of Zhang et al. and Hawker et al. as applied to claims 1-14, 16, 18-19, 21, 33-39, 41-46, 48, and 50 above, and further in view of Leckband et al.

Chapman et al. in view of Zhang et al. and Hawker et al. make obvious a method of making an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles, wherein the polymer brush is formed via surface initiated polymerization of monomers with a core monomer group and a protein resistant head group coupled thereto (see instant 33). This modified reference does not explicitly teach the surface density of polymer. Leckband et al. teach polymer brushes on a substrate as a protein resistant surface (see abstract). In particular, Leckband et al. discuss that the graft density (polymer surface density) is a key parameter in controlling the degree of protein adsorption retardation (see page 1143 paragraph 4). Although Leckband et al. do not provide precise mass per area values for this parameter, they do teach that it is optimized based upon the target environment (e.g. size, geometry and concentration of proteins) (see page 1143

paragraph 4). Thus it would have been well within the purview of one of ordinary skill in the art to optimize such a parameter as a matter of routine experimentation. Therefore claims 33 and 49 are obvious over Chapman et al. in view of Zhang et al., Hawker et al., and Leckband et al.

Response to Arguments

Applicant's arguments, filed June 10, 2008, with respect to the rejection(s) of claims 1, 2, 4, 5, 7-14, 16-19 ,21, 28-37, 39-46, and 48-50 under 35 USC 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new grounds of rejection is made in view of combinations of Chapman et al., Hawker et al, Zhang et al., Healy, Guan et al., and Leckband et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Thursday 8-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

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